

### **Remarks/Arguments**

Claims 58-60 are amended. Claims 1-8, 11, 19, and 58-60 are pending in the application. No new matter has been added. Reexamination and reconsideration of the application, is respectfully requested.

#### **Claim Rejections Under 35 USC § 112, First Paragraph**

Claims 58-60 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

More specifically, the Office Action states that Applicant's specification at page 17 discloses antisense compounds that target a region of the integrin  $\beta 1$  gene, but does not provide support for an artificial intron that targets an exon of any gene. As such, the Office Action states that this is a new matter rejection.

Applicants respectfully submit that the claims have been amended and are directed towards an artificial intron that targets an exon of the integrin  $\beta 1$  gene. As such, the amended claims and specification satisfy the written description requirement because the scope of the claims and the guidance in the specification are sufficient for one skilled in the art to convey that Applicant's had possession of the claimed invention at the time the application was filed.

Applicant respectfully submits that the rejections have been overcome and should be withdrawn.

#### **Claim Rejections Under 35 USC § 102**

Claims 1, 2, 3, 7, 11, and 12 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cheo, et al. (U.S. Pat. No. 7,393,632).

Claim 12 was canceled in an Office Action dated Jun 10, 2008, thus rendering the rejection against the claim moot.

Claims 1, 2, 3, 7, and 11 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cheo. Applicant respectfully traverses this rejection.

Applicant respectfully submits that Cheo fails to disclose an isolated RNA comprising an artificial intron RNA that is released in a cell, thereby silencing the function of a target gene, as set forth by claims 1 and 7. Instead, Cheo discloses methods of making and using RNA interference (RNAi) and antisense RNA to silence genes (col. 112, ll. 19-20). Cheo uses vectors with multiple recombination sites, wherein DNA segments are inserted into a vector so that RNA corresponding to both strands are produced by two separate transcripts (col. 111, ll.39-58). The expression of the DNA sequences results in the production of sense RNA and antisense RNA, which are later hybridized (col. 112, ll. 1-8). Cheo further discloses compounds and methods of using antisense RNA/ribozyme fusions to silence genes (col. 112, ll. 37-46). The fusions are constructed by placing a ribozyme in a vector next to a gene, wherein expression results in the antisense sequence being fused to the ribozyme by an intervening sequence. The intervening sequence may be removed from the transcript using intron and exon splice sequences (col. 112, ll. 47-58). As such, Cheo does not teach or suggest to use artificial intron RNA, that is released in a cell, thereby silencing the function of a target gene, as set forth by claims 1 and 7.

Accordingly, Cheo does not anticipate the present claims 1 and 7. Likewise, dependent claims 2-3 and 11 are also patentable over Cheo for at least the same reasons as claims 1 and 7. In view of the foregoing, Applicant respectfully requests that the Office withdraw the rejection.

### Claim Rejections Under 35 USC § 103

Claims 1-8, 11, 19, and 58-60 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Cheo, Mitchell, et al. (U.S. Pat. No. 6,013,487), Krawczak, et al. (Hum Genet 1992, Vol. 90: 41-54), Zhuang, et al. (PNAS Vol. 86: 2752-2756), Coolidge, et al. (Nucleic Acid Res., 1997, Vol. 25, No. 4:888-896), and Bennett, et al. (U.S. Pat. No. 6,710,174). Applicant respectfully traverses this rejection.

Applicant respectfully submits that Cheo fails to disclose an isolated RNA comprising an artificial intron RNA that is released in a cell, thereby silencing the function of a target gene and is therefore patentable over Choe for at least the same reasons discussed above with regard to claims 1 and 7.

Mitchell is not seen to remedy the defects of Choe and is cited for its relevance regarding a vector insert of a DNA sequence comprising a model intron (5'-CCACAGC-3') with a 3' splice acceptor site (col. 12, ll. 1-20). Splicing of the intron allows for the detection of mRNA molecules via electrophoresis (col. 12, ll. 30-40). Mitchell uses the vector insert comprising the intron to make therapeutic mRNA (th-mRNA), which codes for a protein that has a therapeutic effect (abstract; col. 3, l. 64 to col. 4, l. 4).

Krawczak is not seen to remedy the defects of Choe and Mitchell and is cited for its relevance regarding a donor splice site consensus sequence comprising AGGTAAGT (p. 41, col. 2, last para.). Krawczak uses this consensus sequence to study the spectrum of point mutations in mRNA splice junctions in human genes (abstract).

Zhuang is not seen to remedy the defects of Choe, Mitchell, and Krawczak and is cited for its relevance regarding a known conserved branch site (UACUAAC) that is found in mammalian mRNA splicing (abstract).

Coolidge is not seen to remedy the defects of Choe, Mitchell, Krawczak, and Zhuang and is cited for its relevance regarding the use of poly-pyrimidine tract in pre-mRNA splicing (abstract).

Bennett is not seen to remedy the defects of Choe, Mitchell, Krawczak, Zhuang, and Coolidge and is cited for its relevance regarding the use of antisense oligonucleotides for the modulation of the function of VEGF-1 (abstract). Bennett further states that an intron-exon junction may be a target region for the antisense compounds (col. 7, ll. 1-14).

As such, the combined teachings of the prior art fail to teach or suggest each element of the claimed invention. Likewise, the combined teachings do not teach or suggest to use 1) artificial intron RNA, that is released in a cell, thereby silencing the function of a target gene, as set forth by claims 1 and 7-8 or 2) artificial intron RNA that targets the exon of integrin  $\beta 1$ , as set forth by claim 58-60. Thus, the combination suggested by the Office cannot render the claimed invention obvious.

Likewise, dependent claims 2-6, 11, and 19 also patentable over the cited art for at least the same reasons as claims 1, 7-8, and 58-60.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned at the Los Angeles, California telephone number (310)785-4600 to discuss the steps necessary for placing the application in condition for allowance.

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Amdt. Dated April 16, 2010  
Reply to Office Action of October 16, 2009

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If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,  
HOGAN & HARTSON L.L.P.

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By: 

Natalie A. Davis, Ph.D.  
Registration No. 53,849  
For Applicant(s)

1999 Avenue of the Stars, Suite 1400  
Los Angeles, California 90067  
Telephone: 310-785-4600  
Facsimile: 310-785-4601